CLAIMS

What is claimed is:

1. A method for identifying an anti-viral agent comprising:

contacting a NS4B nucleotide binding motif (NBM) polypeptide with a candidate agent; and

determining an effect of said candidate agent on a nucleotide binding activity, a nucleotide hydrolyzing activity, or a nucleotide-dependent RNA binding activity of said polypeptide.

2. The method of claim 1, wherein said NS4B NBM polypeptide is a hepatitis C virus (HCV) NS4B NBM polypeptide

3. The method of claim 1, wherein said determining comprises determining an effect of said candidate agent on nucleotide binding of said polypeptide.

4. The method of claim 1, wherein said determining comprises determining an effect of said candidate agent on an ability of said polypeptide to hydrolyze a nucleotide.

5. The method of claim 1, wherein said determining comprises determining an effect on an RNA binding activity of said polypeptide.

6. The method of claim 1, wherein said candidate agent is a nucleotide analog.

7. The method of claim 6, wherein said nucleotide analog is a non-hydrolysable nucleotide.

8. The method of claim 1, further comprising determining an effect of said candidate agent on replication of HCV.

9. The method of claim 4, wherein said HCV is a subgenomic or full length HCV replicon.

10. The method of claim 1, further comprising testing HCV replication in a huh7 cell.

11. A method for modulating NS4B protein activity, said method comprising:

contacting said NS4B protein with a modulatory agent in an amount sufficient to modulate a nucleotide binding activity, a nucleotide hydrolyzing activity, or an RNA binding activity of said NS4B protein.

12. A method of inhibiting HCV replication in a cell, comprising:

contacting a cell infected with HCV with an NS4B polypeptide inhibitor, wherein said contacting inhibits a nucleotide binding activity, a nucleotide hydrolyzing activity, or an RNA binding activity of said NS4B polypeptide of said HCV and thereby inhibits HCV replication in said cell.

13. The method of claim 12, wherein said HCV is an HCV subgenomic replicon.

14. The method of claim 12, wherein said cell is a huh7 cell.

15. A polynucleotide encoding a HCV NS4B protein with reduced nucleotide binding activity.

16. The polynucleotide of claim 15, wherein said polynucleotide encodes a polypeptide comprising the sequence $X_1X_2X_3X_4X_5X_6X_7$, where X_1 is an amino acid other than Gly, X_2 is an amino acid other than Ser or Gly, X_3 is an amino acid other than Ile or Val, X_4 is an amino acid other than Gly, X_5 is an amino acid other than Leu or Ile, X6 is an amino acid other than Gly and X_7 is an amino acid other than Lys or Arg.

17. A virus particle containing the polynucleotide of claim 15.

18. A method of treating a subject for hepatitis C, comprising:

administering to said subject an agent that inhibits nucleotide binding activity, a nucleotide hydrolyzing activity, or an RNA binding activity of an HCV NS4B polypeptide in an amount effective for the treatment of said subject.

19. The method of claim 18, wherein said subject is a human subject.

20. The method of claim 18, wherein said agent is administered in combination with another anti-HCV agent.

21. The method of claim 20, wherein said agent is ribavirin or interferon.